IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No.:	**07/ 978,891**	Group Art Unit:	1644
Confirmation No.:	4493	Examiner:	R.B. Schwadron
Filed:	13 November 1992		
Applicant:	Darrell R. ANDERSON *et al.*		

For: Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma

Mail Stop **Petition**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.137(b) TO REVIVE

AN UNINTENTIONALLY ABANDONED APPLICATION FOR COPENDENCY

Sir:

In connection with the recent evaluation of a petition in a pending application (serial no. 09/911,703) that claims priority to the captioned application, serial no. 07/978,891, it has come to applicant's attention that application serial no. 07/978,891 may have become abandoned through unintentional delay before a continuing application, serial no. 08/149,099, now U.S. Patent No. 5,736,137, was filed. In particular, the '891 application may have become abandoned as early as 16 September 1993, whereas the '099 application was filed as a continuation-in-part of the '891 application on 3 November 1993. The record demonstrates that applicant intended, and the Office proceeded under the assumption, that the '099 application was filed prior to the abandonment of the '891 application. Accordingly, applicant petitions under 37 C.F.R. § 1.137(b) to revive the captioned '891 application solely for the purpose of establishing copendency with the '099 application.

The Director is requested to debit the required petition fee of **$1,540** (§ 1.17(m)) from our **Deposit Account No. 18-1260.** Any other fee required for entry or consideration of this paper may be charged to the same account.

Facts

1. Application serial no. 07/978,891 was an original application filed on 13 November 1992. The transmittal papers for the application requested the Commissioner to "[p]lease charge any additional fees or credit any overpayment to" the assignee's deposit account.

2. Following exchanges concerning formalities, the Office mailed a first action on the merits on 15 June 1993 (Paper No. 11). The Office action was nonfinal and set a 3-month period for response. The last day for filing a timely reply without an extension of time was 15 September 1993.

3. Applicant did not file a reply to the first action. Instead, on 3 November 1993, applicant filed application serial no. 08/149,099 as a continuing application claiming priority under 35 U.S.C. § 120 to the '891 application. The transmittal papers for the '099 application, annexed as Attachment A, stated that "[t]his application is a Continuation-in-Part of US Serial Number 07/978,891, filed on November 13, 1993 [*sic*, 1992] (pending) ..." (emphasis added). Additionally, the first page of the specification of the '099 application as filed, annexed as Attachment B, stated that "[t]his is a Continuation-in-Part of United States Serial No. 07/978,891, filed November 13, 1992, pending" (emphasis added).

4. On 7 December 1993, the examiner of the '891 application contacted applicant by telephone. The examiner's interview summary (Paper No. 13) stated that "Applicant notified Examiner that case will be abandoned" (emphasis added).

5. On 15 December 1993, applicant's representative executed and mailed a paper titled "Express Abandonment of Patent Application Under 37 CFR 1.138." The paper referred to the filing of the continuation-in-part application on 3 November 1993 and stated, "in an effort to focus attention and resources on the CIP, Applicants have opted to abandon the present application in favor of the CIP." The paper further stated that "an Official Action issued in this case on June 15, 1992; a response thereto will not be filed." The paper was received by the PTO on 20 December 1993 and entered in the file wrapper as Paper No. 15.

6. On 17 December 1993, the Office mailed a notice of abandonment (Paper No. 14). The examiner indicated that the application was abandoned in view of "Applicant's failure to respond to the Office letter, mailed 6/15/93."

7. The continuation data recorded in the file wrapper of the continuation-in-part application, serial no. 08,149,099, indicates that the Office recognized applicant's claim for priority to the '891 application under § 120. The '099 application was examined by the same examiner, Examiner Schwadron, who was the examiner of record of the '891 application. The '099 application matured to U.S. Patent No. 5,736,137 on 7 April 1998. The face of the '137 patent, annexed as Attachment C, states that the patent is a continuation-in-part of the '891 application.

Discussion

As the facts above demonstrate, applicant believed that the '891 application was pending on 3 November 1993, the date that a continuation-in-part application, serial no. 08/149,099, was filed. Notwithstanding this manifest belief, as well as the blanket fee authorization language included in the filing papers for the '891 application, a review of the official file does not show that an extension of time to respond to the Office action mailed on 15 June 1993 was granted during the pendency of the application. Applicant has not been able to identify evidence from its records that a fee was paid under the blanket authority provided in the filing papers that would correspond to a fee for an extension of time to respond to the Office action mailed 15 June 1993. Accordingly, it appears that the '891 application may in fact have become abandoned on 16 September 1993, before both the date that applicant filed a continuing application as well as the date that applicant filed a letter of express abandonment. Applicant therefore considers that it is prudent to petition the Director to revive the application for the limited purpose of ensuring that the copendency requirement of 35 U.S.C. § 120 is met as to application serial no. 08/149,099.

A petition under 37 C.F.R. § 1.137(b) to revive an application that became abandoned as a result of an unintentional delay by the applicant in submitting a reply requires four elements:

(1) The reply required to the outstanding Office action, unless previously filed.

(2) The petition fee required under § 1.17(m).

(3) A statement that the entire delay in filing the required reply, up to the date of filing a grantable petition, was unintentional.

(4) Any terminal disclaimer as required under § 1.137(d).

(1) Reply

The continuing application filed on 3 November 1993 constitutes a reply to the outstanding Office action within the meaning of § 1.137(b)(1). *See* M.P.E.P. § 711.03(c), subsection II.A.

(2) Fee

Payment of the required fee by debit from our deposit account is requested on the first page of this petition. The fee will be tendered electronically when this petition is filed via EFS-web.

(3) Unintentional delay

The undersigned states, on information and belief following reasonable inquiry of the assignee, that the entire delay from the due date for the reply to the Office action mailed on 15 June 1993 until the filing of the present petition was unintentional.

The Manual identifies three intervals of delay that are relevant to consideration of a petition under § 1.137. *See* M.P.E.P. § 711.03(c), subsection II.D.

(A) Delay in the reply that originally resulted in the abandonment. This first period of delay corresponds to time from the end of the original, unextended period for response to the first Office action, 15 September 1993, until the date the continuation-in-part application was filed, 3 November 1993. The record amply and unambiguously documents that it was applicant's affirmative intention to maintain the pendency of the '891 application during that interval:

- The fling papers for the '099 application clearly stated that the '891 application was believed to be "pending."

- The prosecution of the '099 application (now U.S. Patent No. 5,736,137) demonstrates applicant's intention and expectation that the claim under § 120 for benefit of the '891 application would be effective.
- The interview summary dated 7 December 1993 (Paper No. 13) records applicant's representation that the application "will be abandoned" (*i.e.*, sometime after 7 December 1993). This fact reflects applicant's belief that the '891 application was pending on 7 December 1993.
- The paper titled "Express Abandonment" (Paper No. 15), executed on 15 December and filed on 20 December 1993, manifests applicant's intention to abandon the application as of the date the paper was executed, and no sooner. This fact reflects applicant's belief that the '891 application was pending on 15 December 1993.

(B) Delay in filing an initial petition to revive the application. During the interval from 1993 to 2007, neither the assignee of this application nor its representatives were aware that the original '891 application and the CIP '099 application may not have been copending. The record clearly reflects that applicant believed in the first instance that the pendency of the '891 application had been maintained at least until the filing of the '099 application. Applicant stated a claim for priority to the '891 application in several subsequent applications, including those that matured to U.S. Patent Nos. 5,736,137, 5,776,456, 5,843,439, 6,399,061, and 6,682,734, as well as pending application serial nos. 09/911,692, 09/911,703, and 10/238,681. In every case, the Office recognized applicant's claim for priority and treated it as proper. Moreover, every U.S. application claiming priority to the original '891 application has been examined by the same examiner. When prior art has been applied, no question regarding applicant's ability properly to claim priority to the '891 application has been raised. The compliance with the requirements of § 120 of the claim for priority to the original application – which, it was understood, had indeed been abandoned after the '099 CIP application was filed – has never been questioned throughout the examination of these related applications.

Applicant's representatives first became aware in late October, 2007, that the '891 application may have become abandoned before the '099 application was filed. On 29 March 2007, applicant filed a petition under § 1.78(a)(3) to accept a delayed priority claim in

pending application serial no. 09/911,703, which claims priority to the '891 application. (The '703 application was filed in July 2001; an amendment to conform the priority claim in the specification of the '703 application with the formal requirements of § 120 was filed in August 2005; and the examiner advised applicant in an Office action mailed on 29 December 2006 that a petition under § 1.78(a)(3) would be required.) Between April and October of 2007, applicant repeatedly contacted the Office of Petitions to inquire about the status of the petition. In discussions that occurred with personnel in that office in late October and early November, 2007, applicant was advised that a question had arisen concerning the formal sufficiency of the priority claim as to the '891 application. In particular, applicant was informed that the '891 application may not have been pending on the date that the '099 application was filed.

Upon becoming aware of the possibility that the '891 and '099 applications may not have been copending, the undersigned immediately obtained and reviewed a copy of the public record for the '891 application file. Applicant also diligently began a search of its records, including records related to the deposit account identified in the filing papers for the '891 and '099 applications. Applicant is continuing to search these records. Nonetheless, based on discussions with various Office personnel, and to remove the issue from any doubt, applicant and its representatives determined that a petition to revive the '891 application should be filed, and this petition was promptly prepared. Accordingly, no part of the delay between the filing of the '099 application in November 1993 and the filing of the present petition was intentional.

(C) Delay between the filing of an initial petition and a grantable petition under § 1.137. Applicant believes that the present petition complies with the requirements of § 1.137, as explained at M.P.E.P. § 711.03(c), and is therefore grantable as filed.

(4) Terminal disclaimer pursuant to § 1.137(d)

This application was filed before 8 June 1995, and this petition is not filed solely for purposes of copendency with an application filed on or after 8 June 1995. Accordingly, this petition is subject to the requirements of § 1.137(d)(1).

This petition is submitted with a concurrently-filed petition under § 1.183 to waive the terminal disclaimer requirement of § 1.137(b)(4), as discussed at M.P.E.P. § 711.03(c), subsection II.G.

Conclusion

Applicant respectfully requests that application serial no. 07/978,891 be revived solely to establish copendency with application serial no. 08/149,099, filed on 3 November 1993, and that once such copendency has been established, the application again be abandoned.

Respectfully submitted,

/David L. Fitzgerald/

David L. Fitzgerald, Reg. No. 47,347
Attorney for Biogen Idec Inc.

7 November 2007

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ATTACHMENT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Date: 3 November 1993

PATENT APPLICATION TRANSMITTAL LETTER

HONORABLE COMMISSIONER OF PATENTS
AND TRADEMARKS
Box SEQUENCE
Washington D.C. 20231

Transmitted herewith for filing by:

__X__ a. EXPRESS MAIL
_____ b. Hand Delivery

is the

__X__ a. complete
_____ b. incomplete

Patent Application of: ANDERSON, DR; HANNA, N; LEONARD, JE; NEWMAN, RA; REFF, ME; RASTETTER, WH.

Title: THERAPEUTIC APPLICATION OF CHIMERIC AND RADIOLABELED ANTIBODIES TO HUMAN LYMPHOCYTE RESTRICTED DIFFERENTIATION ANTIGEN FOR TREATMENT OF B CELL LYMPHOMA

Executed On: 3 November 1993

This Application is a Continuation-In-Part of US Serial Number 07/978,891, filed on November 13, 1993 (pending) and priority under 35 U.S.C. §120 is hereby claimed.

__X__ 1. An application consisting of **80** pages of specification and claims and **21** sheets of formal/**informal** drawings is attached.

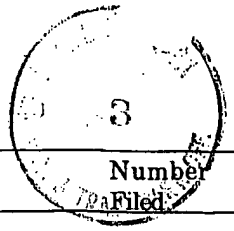
_____ 2a. A Declaration and Power of Attorney is attached.

__X__ 2b. A Declaration and Power of Attorney is not attached. Please file this application in the name of the inventors listed above (full names of all).

__X__ 3. An assignment of the invention to IDEC Pharmaceuticals Corporation will follow .

__X__ 4. A filing date in accordance with 37 C.F.R. 1.10 is requested. The Express Mail Certificate appears below.

__X__ 5. A Small Entity Form is attached.



COMPUTATION OF FEE

	Number Filed		Number Extra	Rate	Basic Fee $710/$355
Total Claims	20	-20=	0	x $22/$11 =	0
Independent Claims	5	-3=	2	x $74/$37 =	$74
Multiple Dependent Claims	0			x $230/$115 =	0
			Total Filing Fee		$429
			Assignment Recording Fee ($8.00)		$
			TOTAL		$429

_____6. Our check no. _____ in the amount of $_____ to cover the total fee as computed above is enclosed.

_____7. No fee is enclosed.

_X__8. Please charge any fees, including those listed in **TOTAL** above, or credit any overpayment to Deposit Account no. 09-0017. A copy of this sheet is enclosed.

Respectfully submitted,

Richard P. Burgoon, Jr.
Reg. No. 34,787
Intellectual Property Counsel
IDEC PHARMACEUTICALS CORPORATION
11011 Torreyana Road
San Diego, CA 92121
(619) 550-8500

EXPRESS MAIL CERTIFICATE

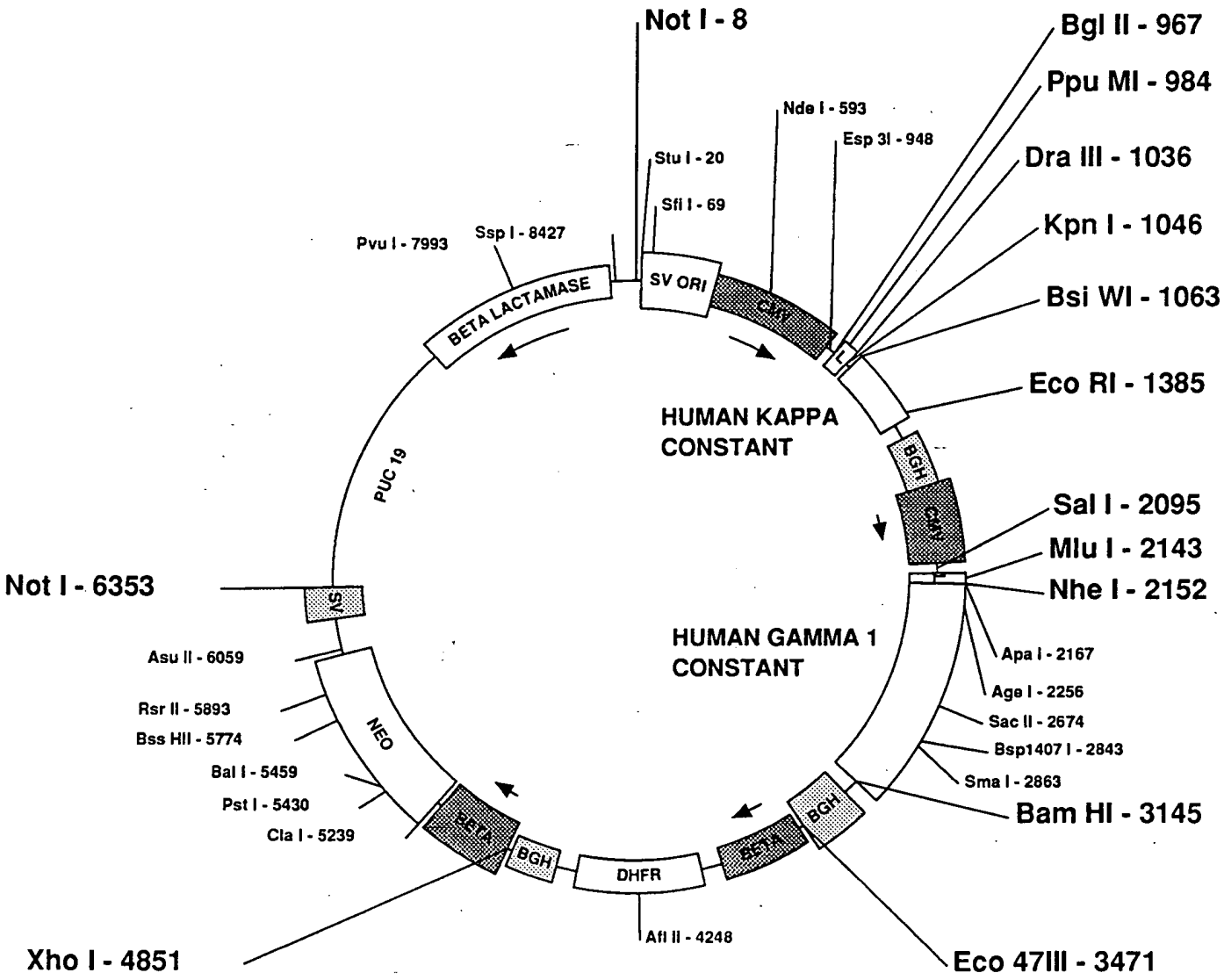
"Express Mail" mailing label number: EF092540446 US
Date of deposit: **3 November 1993**

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Box SEQUENCE, Washington, D.C. 20231.

Mabel R. Hernandez
(Typed or printed name of person mailing paper or fee

Mabel R. Hernandez
(Signature of person mailing paper or fee)

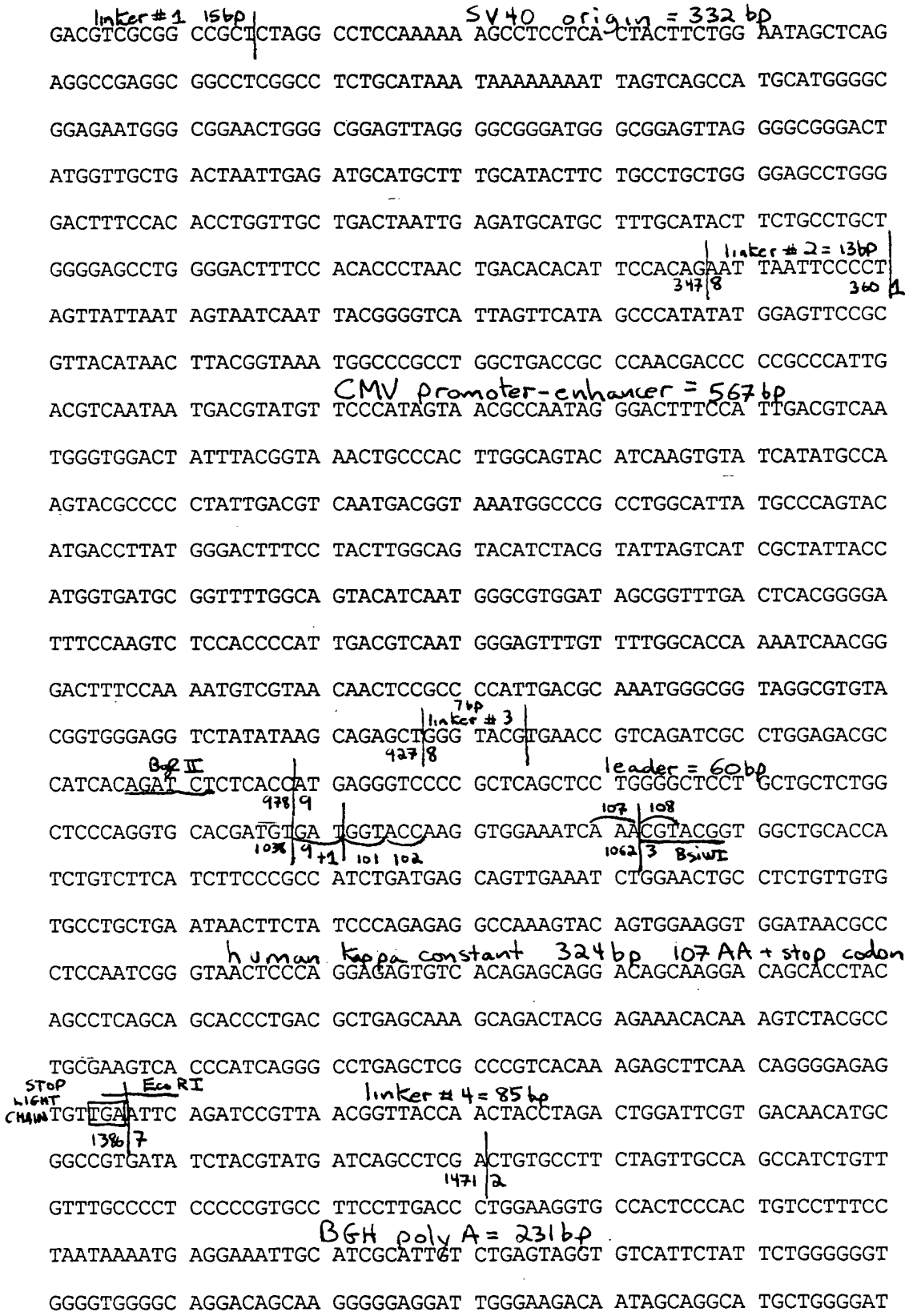
TCAE 8



8540 BP MAP BY MITCHELL REFF 11/6/92

L=Leader,CMV=Cytomegalovirus promoter
BETA=Mouse beta globin major promoter
BGH=Bovine growth hormone polyadenylation
SV=SV40 early polyadenylation
SV ORI=SV40 origin

Noncutters=AscI,AvrII,BspMII,Bst1107I
HindIII,I-PpoI,MamI,MunI,NruI,PacI,PmeI
PmlI,RemI,SgrAI,SpeI,SrfI,Sse8387I,SwaI
XbaI,XcmI

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AGGCCGAGGC GGCCTCGGCC TCTGCATAAA TAAAAAAAAT TAGTCAGCCA TGCATGGGGC    120
GGAGAATGGG CGGAACTGGG CGGAGTTAGG GGCGGGATGG GCGGAGTTAG GGGCGGGACT    180
ATGGTTGCTG ACTAATTGAG ATGCATGCTT TGCATACTTC TGCCTGCTGG GGAGCCTGGG    240
GACTTTCCAC ACCTGGTTGC TGACTAATTG AGATGCATGC TTTGCATACT TCTGCCTGCT    300
GGGGAGCCTG GGGACTTTCC ACACCCTAAC TGACACACAT TCCACAGAAT TAATTCCCCT    360
AGTTATTAAT AGTAATCAAT TACGGGGTCA TTAGTTCATA GCCCATATAT GGAGTTCCGC    420
GTTACATAAC TTACGGTAAA TGGCCCGCCT GGCTGACCGC CCAACGACCC CCGCCCATTG    480
ACGTCAATAA TGACGTATGT TCCCATAGTA ACGCCAATAG GGACTTTCCA TTGACGTCAA    540
TGGGTGGACT ATTTACGGTA AACTGCCCAC TTGGCAGTAC ATCAAGTGTA TCATATGCCA    600
AGTACGCCCC CTATTGACGT CAATGACGGT AAATGGCCCG CCTGGCATTA TGCCCAGTAC    660
ATGACCTTAT GGGACTTTCC TACTTGGCAG TACATCTACG TATTAGTCAT CGCTATTACC    720
ATGGTGATGC GGTTTTGGCA GTACATCAAT GGGCGTGGAT AGCGGTTTGA CTCACGGGGA    780
TTTCCAAGTC TCCACCCCAT TGACGTCAAT GGGAGTTTGT TTTGGCACCA AAATCAACGG    840
GACTTTCCAA AATGTCGTAA CAACTCCGCC CCATTGACGC AAATGGGCGG TAGGCGTGTA    900
CGGTGGGAGG TCTATATAAG CAGAGCTGGG TACGTGAACC GTCAGATCGC CTGGAGACGC    960
CATCACAGAT CTCTCACCAT GAGGGTCCCC GCTCAGCTCC TGGGGCTCCT GCTGCTCTGG   1020
CTCCCAGGTG CACGATGTGA TGGTACCAAG GTGGAAATCA AACGTACGGT GGCTGCACCA   1080
TCTGTCTTCA TCTTCCCGCC ATCTGATGAG CAGTTGAAAT CTGGAACTGC CTCTGTTGTG   1140
TGCCTGCTGA ATAACTTCTA TCCCAGAGAG GCCAAAGTAC AGTGGAAGGT GGATAACGCC   1200
CTCCAATCGG GTAACTCCCA GGAGAGTGTC ACAGAGCAGG ACAGCAAGGA CAGCACCTAC   1260
AGCCTCAGCA GCACCCTGAC GCTGAGCAAA GCAGACTACG AGAAACACAA AGTCTACGCC   1320
TGCGAAGTCA CCCATCAGGG CCTGAGCTCG CCCGTCACAA AGAGCTTCAA CAGGGGAGAG   1380
TGTTGAATTC AGATCCGTTA ACGGTTACCA ACTACCTAGA CTGGATTCGT GACAACATGC   1440
GGCCGTGATA TCTACGTATG ATCAGCCTCG ACTGTGCCTT CTAGTTGCCA GCCATCTGTT   1500
GTTTGCCCCT CCCCCGTGCC TTCCTTGACC CTGGAAGGTG CCACTCCCAC TGTCCTTTCC   1560
TAATAAAATG AGGAAATTGC ATCGCATTGT CTGAGTAGGT GTCATTCTAT TCTGGGGGGT   1620
GGGGTGGGGC AGGACAGCAA GGGGGAGGAT TGGGAAGACA ATAGCAGGCA TGCTGGGGAT   1680
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linker #5 = 15bp

GCGGTGGGCT CTATGGAACC AGCTGGGGCT CGACAGCTAT GCCAAGTACG CCCCCTATTG 1740

1702|3 1717|8

ACGTCAATGA CGGTAAATGG CCCGCCTGGC ATTATGCCCA GTACATGACC TTATGGGACT 1800

TTCCTACTTG GCAGTACATC TACGTATTAG TCATCGCTAT TACCATGGTG ATGCGGTTTT 1860

CMV promoter-enhancer = 334bp

GGCAGTACAT CAATGGGCGT GGATAGCGGT TTGACTCACG GGGATTTCCA AGTCTCCACC 1920

CCATTGACGT CAATGGGAGT TTGTTTTGGC ACCAAAATCA ACGGGACTTT CCAAAATGTC 1980

GTAACAACTC CGCCCCATTG ACGCAAATGG GCGGTAGGCG TGTACGGTGG GAGGTCTATA 2040

linker #6 76bp

TAAGCAGAGC TGGGTACGTC CTCACATTCA GTGATCAGCA CTGAACACAG ACCCGTCGAC 2100

Sal 1

2051|2 2058|9

MluI

ATGGGTTGGA GCCTCATCTT GCTCTTCCTT GTCGCTGTTG CTACGCGTGT CGCTAGCACC 2160

leader = 51bp 2151|2 NheI

2100|1 START heavy chain -5 -4 -3 114 115

AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG 2220

GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA 2280

GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC 2340

human gamma 1 constant

TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC 2400

993 bp = 330 AA + stop codon

AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGCAGAGCC CAAATCTTGT 2460

GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC 2520

TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA 2580

TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC 2640

GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC 2700

CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG 2760

TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA 2820

GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG 2880

AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG 2940

TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC 3000

GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG 3060

AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC 3120

STOP BamH1 linker #7 = 81 bp

CTCTCCCTGT CTCCGGGTAA ATGAGGATCC GTTAACGGTT ACCAACTACC TAGACTGGAT 3180

heavy chain 3144|5

TCGTGACAAC ATGCGGCCGT GATATCTACG TATGATCAGC CTCGACTGTG CCTTCTAGTT 3240

3225|6

GCCAGCCATC TGTTGTTTGC CCCTCCCCCG TGCCTTCCTT GACCCTGGAA GGTGCCACTC 3300

Bovine growth hormone polyadenylation region = 231bp

CCACTGTCCT TTCCTAATAA AATGAGGAAA TTGCATCGCA TTGTCTGAGT AGGTGTCATT 3360

CTATTCTGGG GGGTGGGGTG GGGCAGGACA GCAAGGGGGA GGATTGGGAA GACAATAGCA 3420

linker # 8 = 34 bp

GGCATGCTGG GGATGCGGTG GGCTCTATGG AACCAGCTGG GGCTCGACAG CGCTGGATCT 3480

3456|7

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CCCGATCCCC|AGCTTTGCTT CTCAATTTCT TATTTGCATA ATGAGAAAAA AAGGAAAATT   3540
    3490|1
AATTTTAACA CCAATTCAGT AGTTGATTGA GCAAATGCGT TGCCAAAAAG GATGCTTTAG   3600
        Mouse Beta globin major promter = 366bp
AGACAGTGTT CTCTGCACAG ATAAGGACAA ACATTATTCA GAGGGAGTAC CCAGAGCTGA   3660

GACTCCTAAG CCAGTGAGTG GCACAGCATT CTAGGGAGAA ATATGCTTGT CATCACCGAA   3720

GCCTGATTCC GTAGAGCCAC ACCTTGGTAA GGGCCAATCT GCTCACACAG GATAGAGAGG   3780

GCAGGAGCCA GGGCAGAGCA TATAAGGTGA GGTAGGATCA GTTGCTCCTC ACATTTGCTT   3840
          | linker # 9 = 196bp          | 5' untranslated DHFR = 826bp
CTGACATAGT TGTGTTGGGA GCTTGGATAG CTTGGACAGC TCAGGGCTGC GATTTCGCGC   3900
          3852|7                    3875|6
                                                  | START DHFR
CAAACTTGAC GGCAATCCTA GCGTGAAGGC TGGTAGGATT TTATCCCCGC TGCCATCATG   3960
                                                    3957|8
GTTCGACCAT TGAACTGCAT CGTCGCCGTG TCCCAAAATA TGGGGATTGG CAAGAACGGA   4020

GACCTACCCT GGCCTCCGCT CAGGAACGAG TTCAAGTACT TCCAAAGAAT GACCACAACC   4080

TCTTCAGTGG AAGGTAAACA GAATCTGGTG ATTATGGGTA GGAAAACCTG GTTCTCCATT   4140
    Mouse DHFR = 564 bp = 187 amino acids + stop codon
CCTGAGAAGA ATCGACCTTT AAAGGACAGA ATTAATATAG TTCTCAGTAG AGAACTCAAA   4200

GAACCACCAC GAGGAGCTCA TTTTCTTGCC AAAAGTTTGG ATGATGCCTT AAGACTTATT   4260

GAACAACCGG AATTGGCAAG TAAAGTAGAC ATGGTTTGGA TAGTCGGAGG CAGTTCTGTT   4320

TACCAGGAAG CCATGAATCA ACCAGGCCAC CTTAGACTCT TTGTGACAAG GATCATGCAG   4380

GAATTTGAAA GTGACACGTT TTTCCCAGAA ATTGATTTGG GGAAATATAA ACTTCTCCCA   4440

GAATACCCAG GCGTCCTCTC TGAGGTCCAG GAGGAAAAAG GCATCAAGTA TAAGTTTGAA   4500
      STOP DHFR  4521|2
GTCTACGAGA AGAAAGACTA ACAGGAAGAT GCTTTCAAGT TCTCTGCTCC CCTCCTAAAG   4560
3' untranslated DHFR = 826bp                  |linker # 10 = 106bp|
CTATGCATTT TTATAAGACC ATGGGACTTT TGCTGGCTTT AGATCAGCCT CGACTGTGCC   4620
                                          4603|4      4637|4
TTCTAGTTGC CAGCCATCTG TTGTTTGCCC CTCCCCCGTG CCTTCCTTGA CCCTGGAAGG   4680
    Bovine growth hormone polyadenylation region = 231bp
TGCCACTCCC ACTGTCCTTT CCTAATAAAA TGAGGAAATT GCATCGCATT GTCTGAGTAG   4740

GTGTCATTCT ATTCTGGGGG GTGGGGTGGG GCAGGACAGC AAGGGGGAGG ATTGGGAAGA   4800

                                          | linker # 11 = 17bp
CAATAGCAGG CATGCTGGGG ATGCGGTGGG CTCTATGGAA CCAGCTGGGG CTCGAGCTAC   4860
                                          4844|5
|
TAGCTTTGCT TCTCAATTTC TTATTTGCAT AATGAGAAAA AAAGGAAAAT TAATTTTAAC   4920
4861|2
ACCAATTCAG TAGTTGATTG AGCAAATGCG TTGCCAAAAA GGATGCTTTA GAGACAGTGT   4980
                Mouse beta globin major promoter = 366bp
TCTCTGCACA GATAAGGACA AACATTATTC AGAGGGAGTA CCCAGAGCTG AGACTCCTAA   5040

GCCAGTGAGT GGCACAGCAT TCTAGGGAGA AATATGCTTG TCATCACCGA AGCCTGATTC   5100

CGTAGAGCCA CACCTTGGTA AGGGCCAATC TGCTCACACA GGATAGAGAG GGCAGGAGCC   5160

AGGGCAGAGC ATATAAGGTG AGGTAGGATC AGTTGCTCCT CACATTTGCT TCTGACATAG   5220
          | linker # 12 = 216bp                | START NEO
TTGTGTTGGG AGCTTGGATC GATCCTCCAT GGTTGAACAA GATGGATTGC ACGCAGGTTC   5280
          5227|8                  5248|9
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Figure 2 (cont.)


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TCCGGCCGCT TGGGTGGAGA GGCTATTCGG CTATGACTGG GCACAACAGA CAATCGGCTG   5340

CTCTGATGCC GCCGTGTTCC GGCTGTCAGC GCAGGGGCGC CCGGTTCTTT TTGTCAAGAC   5400

                Neomycin phosphotransferase
CGACCTGTCC GGTGCCCTGA ATGAACTGCA GGACGAGGCA GCGCGGCTAT CGTGGCTGGC   5460

                795 bp = 264 amino acids + stop codon
CACGACGGGC GTTCCTTGCG CAGCTGTGCT CGACGTTGTC ACTGAAGCGG GAAGGGACTG   5520

GCTGCTATTG GGCGAAGTGC CGGGGCAGGA TCTCCTGTCA TCTCACCTTG CTCCTGCCGA   5580

GAAAGTATCC ATCATGGCTG ATGCAATGCG GCGGCTGCAT ACGCTTGATC CGGCTACCTG   5640

CCCATTCGAC CACCAAGCGA AACATCGCAT CGAGCGAGCA CGTACTCGGA TGGAAGCCGG   5700

TCTTGTCGAT CAGGATGATC TGGACGAAGA GCATCAGGGG CTCGCGCCAG CCGAACTGTT   5760

CGCCAGGCTC AAGGCGCGCA TGCCCGACGG CGAGGATCTC GTCGTGACCC ATGGCGATGC   5820

CTGCTTGCCG AATATCATGG TGGAAAATGG CCGCTTTTCT GGATTCATCG ACTGTGGCCG   5880

GCTGGGTGTG GCGGACCGCT ATCAGGACAT AGCGTTGGCT ACCCGTGATA TTGCTGAAGA   5940

GCTTGGCGGC GAATGGGCTG ACCGCTTCCT CGTGCTTTAC GGTATCGCCG CTCCCGATTC   6000

                STOP NEO
GCAGCGCATC GCCTTCTATC GCCTTCTTGA CGAGTTCTTC TGA|GCGGGAC TCTGGGGTTC   6060
                                              6043|4

GAAATGACCG ACCAAGCGAC GCCCAACCTG CCATCACGAG ATTTCGATTC CACCGCCGCC   6120

                3' untranslated NEO = 173 bp
TTCTATGAAA GGTTGGGCTT CGGAATCGTT TTCCGGGACG CCGGCTGGAT GATCCTCCAG   6180

CGCGGGGATC TCATGCTGGA GTTCTTCGCC CACCCC|AACT TGTTTATTGC AGCTTATAAT   6240
                                     6216|7

GGTTACAAAT AAAGCAATAG CATCACAAAT TTCACAAATA AAGCATTTTT TTCACTGCAT   6300

                SV40 poly A early = 133 bp          linker #13 = 19bp
TCTAGTTGTG GTTTGTCCAA ACTCATCAAT CTATCTTATC ATGTCTGGAT CGCGGCCGCG   6360
                                              6349|50

ATCCCGTC|GA GAGCTTGGCG TAATCATGGT CATAGCTGTT TCCTGTGTGA AATTGTTATC   6420
      6368|9

CGCTCACAAT TCCACACAAC ATACGAGCCG GAAGCATAAA GTGTAAAGCC TGGGGTGCCT   6480

AATGAGTGAG CTAACTCACA TTAATTGCGT TGCGCTCACT GCCCGCTTTC CAGTCGGGAA   6540

ACCTGTCGTG CCAGCTGCAT TAATGAATCG GCCAACGCGC GGGGAGAGGC GGTTTGCGTA   6600

                PUC 19
TTGGGCGCTC TTCCGCTTCC TCGCTCACTG ACTCGCTGCG CTCGGTCGTT CGGCTGCGGC   6660

GAGCGGTATC AGCTCACTCA AAGGCGGTAA TACGGTTATC CACAGAATCA GGGGATAACG   6720

CAGGAAAGAA CATGTGAGCA AAAGGCCAGC AAAAGGCCAG GAACCGTAAA AAGGCCGCGT   6780

                6792= bacterial origin of replication
TGCTGGCGTT T[T]TCCATAGG CTCCGCCCCC CTGACGAGCA TCACAAAAAT CGACGCTCAA   6840

GTCAGAGGTG GCGAAACCCG ACAGGACTAT AAAGATACCA GGCGTTTCCC CCTGGAAGCT   6900

CCCTCGTGCG CTCTCCTGTT CCGACCCTGC CGCTTACCGG ATACCTGTCC GCCTTTCTCC   6960

CTTCGGGAAG CGTGGCGCTT TCTCAATGCT CACGCTGTAG GTATCTCAGT TCGGTGTAGG   7020

TCGTTCGCTC CAAGCTGGGC TGTGTGCACG AACCCCCCGT TCAGCCCGAC CGCTGCGCCT   7080
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Figure 2 (cont.)


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TATCCGGTAA CTATCGTCTT GAGTCCAACC CGGTAAGACA CGACTTATCG CCACTGGCAG   7140

CAGCCACTGG TAACAGGATT AGCAGAGCGA GGTATGTAGG CGGTGCTACA GAGTTCTTGA   7200

AGTGGTGGCC TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGCTGA   7260

AGCCAGTTAC CTTCGGAAAA AGAGTTGGTA GCTCTTGATC CGGCAAACAA ACCACCGCTG   7320

GTAGCGGTGG TTTTTTTGTT TGCAAGCAGC AGATTACGCG CAGAAAAAAA GGATCTCAAG   7380

AAGATCCTTT GATCTTTTCT ACGGGGTCTG ACGCTCAGTG GAACGAAAAC TCACGTTAAG   7440

GGATTTTGGT CATGAGATTA TCAAAAAGGA TCTTCACCTA GATCCTTTTA AATTAAAAAT   7500

                                                  7550 = stop
GAAGTTTTAA ATCAATCTAA AGTATATATG AGTAAACTTG GTCTGACAGT TACCAATGCT   7560
                                                  Beta lactamase

TAATCAGTGA GGCACCTATC TCAGCGATCT GTCTATTTCG TTCATCCATA GTTGCCTGAC   7620

TCCCCGTCGT GTAGATAACT ACGATACGGG AGGGCTTACC ATCTGGCCCC AGTGCTGCAA   7680

TGATACCGCG AGACCCACGC TCACCGGCTC CAGATTTATC AGCAATAAAC CAGCCAGCCG   7740

                Beta lactamase = 861bp
GAAGGGCCGA GCGCAGAAGT GGTCCTGCAA CTTTATCCGC CTCCATCCAG TCTATTAATT   7800

                286 amino acid + stop codon
GTTGCCGGGA AGCTAGAGTA AGTAGTTCGC CAGTTAATAG TTTGCGCAAC GTTGTTGCCA   7860

TTGCTACAGG CATCGTGGTG TCACGCTCGT CGTTTGGTAT GGCTTCATTC AGCTCCGGTT   7920

CCCAACGATC AAGGCGAGTT ACATGATCCC CCATGTTGTG CAAAAAAGCG GTTAGCTCCT   7980

TCGGTCCTCC GATCGTTGTC AGAAGTAAGT TGGCCGCAGT GTTATCACTC ATGGTTATGG   8040

CAGCACTGCA TAATTCTCTT ACTGTCATGC CATCCGTAAG ATGCTTTTCT GTGACTGGTG   8100

AGTACTCAAC CAAGTCATTC TGAGAATAGT GTATGCGGCG ACCGAGTTGC TCTTGCCCGG   8160

CGTCAATACG GGATAATACC GCGCCACATA GCAGAACTTT AAAAGTGCTC ATCATTGGAA   8220

AACGTTCTTC GGGGCGAAAA CTCTCAAGGA TCTTACCGCT GTTGAGATCC AGTTCGATGT   8280

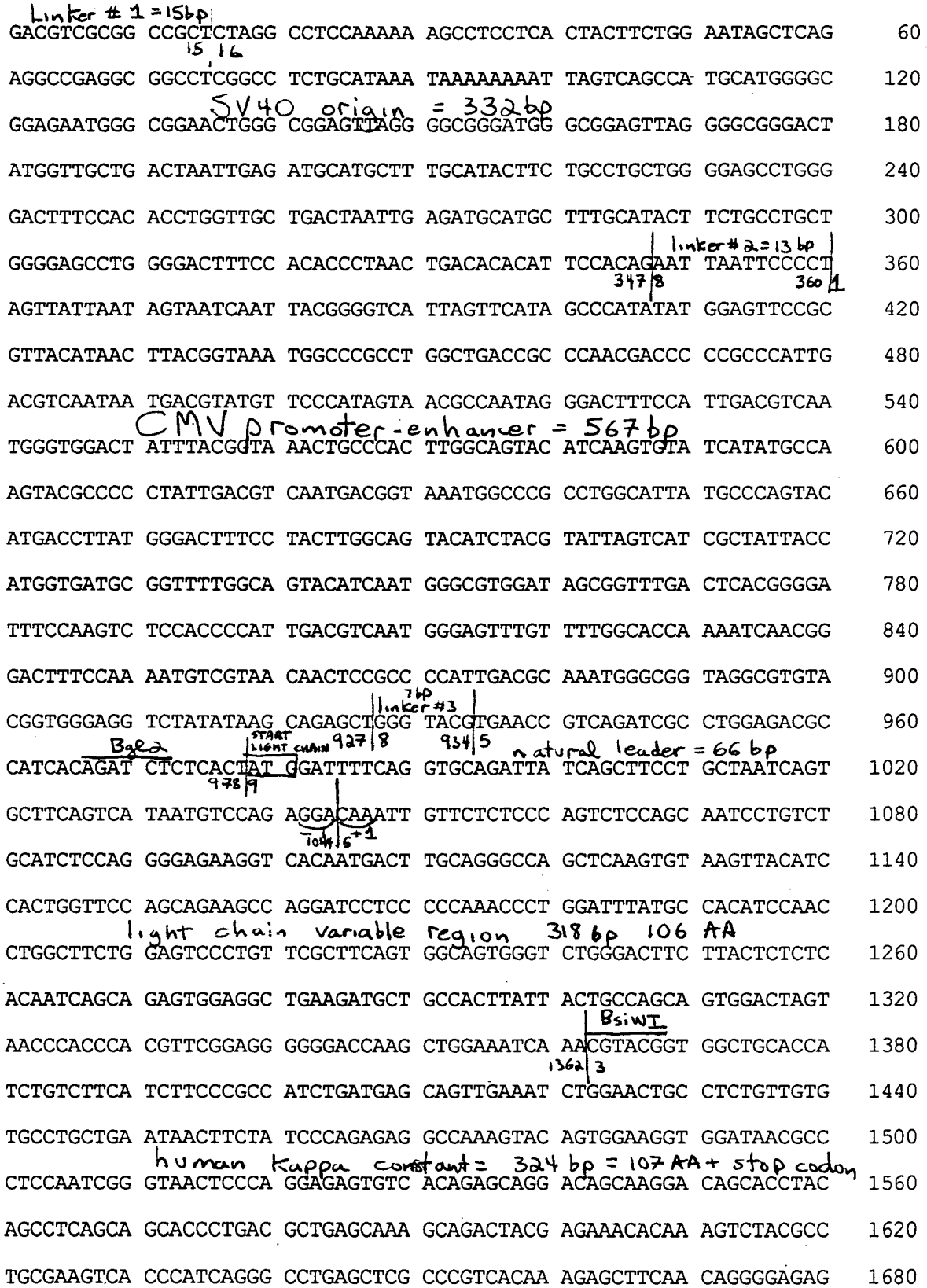
AACCCACTCG TGCACCCAAC TGATCTTCAG CATCTTTTAC TTTCACCAGC GTTTCTGGGT   8340

GAGCAAAAAC AGGAAGGCAA AATGCCGCAA AAAAGGGAAT AAGGGCGACA CGGAAATGTT   8400

      8410 = start Beta lactamase
GAATACTCAT ACTCTTCCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGTCTCA   8460

TGAGCGGATA CATATTTGAA TGTATTTAGA AAAATAAACA AATAGGGGTT CCGCGCACAT   8520

TTCCCCGAAA AGTGCCACCT
```



GACGTCGCGG CCGCTCTAGG CCTCCAAAAA AGCCTCCTCA CTACTTCTGG AATAGCTCAG 60

AGGCCGAGGC GGCCTCGGCC TCTGCATAAA TAAAAAAAAT TAGTCAGCCA TGCATGGGGC 120

GGAGAATGGG CGGAACTGGG CGGAGTTAGG GGCGGGATGG GCGGAGTTAG GGGCGGGACT 180

ATGGTTGCTG ACTAATTGAG ATGCATGCTT TGCATACTTC TGCCTGCTGG GGAGCCTGGG 240

GACTTTCCAC ACCTGGTTGC TGACTAATTG AGATGCATGC TTTGCATACT TCTGCCTGCT 300

GGGGAGCCTG GGGACTTTCC ACACCCTAAC TGACACACAT TCCACAGAAT TAATTCCCCT 360

AGTTATTAAT AGTAATCAAT TACGGGGTCA TTAGTTCATA GCCCATATAT GGAGTTCCGC 420

GTTACATAAC TTACGGTAAA TGGCCCGCCT GGCTGACCGC CCAACGACCC CCGCCCATTG 480

ACGTCAATAA TGACGTATGT TCCCATAGTA ACGCCAATAG GGACTTTCCA TTGACGTCAA 540

TGGGTGGACT ATTTACGGTA AACTGCCCAC TTGGCAGTAC ATCAAGTGTA TCATATGCCA 600

AGTACGCCCC CTATTGACGT CAATGACGGT AAATGGCCCG CCTGGCATTA TGCCCAGTAC 660

ATGACCTTAT GGGACTTTCC TACTTGGCAG TACATCTACG TATTAGTCAT CGCTATTACC 720

ATGGTGATGC GGTTTTGGCA GTACATCAAT GGGCGTGGAT AGCGGTTTGA CTCACGGGGA 780

TTTCCAAGTC TCCACCCCAT TGACGTCAAT GGGAGTTTGT TTTGGCACCA AAATCAACGG 840

GACTTTCCAA AATGTCGTAA CAACTCCGCC CCATTGACGC AAATGGGCGG TAGGCGTGTA 900

CGGTGGGAGG TCTATATAAG CAGAGCTGGG TACGTGAACC GTCAGATCGC CTGGAGACGC 960

CATCACAGAT CTCTCACTAT GGATTTTCAG GTGCAGATTA TCAGCTTCCT GCTAATCAGT 1020

GCTTCAGTCA TAATGTCCAG AGGACAAATT GTTCTCTCCC AGTCTCCAGC AATCCTGTCT 1080

GCATCTCCAG GGGAGAAGGT CACAATGACT TGCAGGGCCA GCTCAAGTGT AAGTTACATC 1140

CACTGGTTCC AGCAGAAGCC AGGATCCTCC CCCAAACCCT GGATTTATGC CACATCCAAC 1200

CTGGCTTCTG GAGTCCCTGT TCGCTTCAGT GGCAGTGGGT CTGGGACTTC TTACTCTCTC 1260

ACAATCAGCA GAGTGGAGGC TGAAGATGCT GCCACTTATT ACTGCCAGCA GTGGACTAGT 1320

AACCCACCCA CGTTCGGAGG GGGGACCAAG CTGGAAATCA AACGTACGGT GGCTGCACCA 1380

TCTGTCTTCA TCTTCCCGCC ATCTGATGAG CAGTTGAAAT CTGGAACTGC CTCTGTTGTG 1440

TGCCTGCTGA ATAACTTCTA TCCCAGAGAG GCCAAAGTAC AGTGGAAGGT GGATAACGCC 1500

CTCCAATCGG GTAACTCCCA GGAGAGTGTC ACAGAGCAGG ACAGCAAGGA CAGCACCTAC 1560

AGCCTCAGCA GCACCCTGAC GCTGAGCAAA GCAGACTACG AGAAACACAA AGTCTACGCC 1620

TGCGAAGTCA CCCATCAGGG CCTGAGCTCG CCCGTCACAA AGAGCTTCAA CAGGGGAGAG 1680

STOP LIGHT CHAIN | EcoR1 linker #4 = 81 bp

TGTTGAATTC AGATCCGTTA ACGGTTACCA ACTACCTAGA CTGGATTCGT GACAACATGC 1740

1686 | 7

GGCCGTGATA TCTACGTATG ATCAGCCTCG ACTGTGCCTT CTAGTTGCCA GCCATCTGTT 1800

1771 | 2

GTTTGCCCCT CCCCCGTGCC TTCCTTGACC CTGGAAGGTG CCACTCCCAC TGTCCTTTCC 1860

TAATAAAATG AGGAAATTGC ATCGCATTGT CTGAGTAGGT GTCATTCTAT TCTGGGGGGT 1920

Bovine growth hormone polyadenylation region = 231 bp

GGGGTGGGGC AGGACAGCAA GGGGGAGGAT TGGGAAGACA ATAGCAGGCA TGCTGGGGAT 1980

linker #5 = 15 bp

GCGGTGGGCT CTATGGAACC AGCTGGGGCT CGACAGCTAT GCCAAGTACG CCCCCTATTG 2040

2002 | 3 2017 | 8

ACGTCAATGA CGGTAAATGG CCCGCCTGGC ATTATGCCCA GTACATGACC TTATGGGACT 2100

TTCCTACTTG GCAGTACATC TACGTATTAG TCATCGCTAT TACCATGGTG ATGCGGTTTT 2160

CMV Promoter-enhancer = 334 bp

GGCAGTACAT CAATGGGCGT GGATAGCGGT TTGACTCACG GGGATTTCCA AGTCTCCACC 2220

CCATTGACGT CAATGGGAGT TTGTTTTGGC ACCAAAATCA ACGGGACTTT CCAAAATGTC 2280

GTAACAACTC CGCCCCATTG ACGCAAATGG GCGGTAGGCG TGTACGGTGG GAGGTCTATA 2340

7 bp linker #6 Sal1

TAAGCAGAGC TGGGTACGTC CTCACATTCA GTGATCAGCA CTGAACACAG ACCCGTCGAC 2400

2351 | 2 2358 | 9 Synthetic + natural leader Mlu1 2457 | 8

start heavy chain

ATGGGTTGGA GCCTCATCTT GCTCTTCCTT GTCGCTGTTG CTACGCGTGT CCTGTCCCAG 2460

2400 | 1 -5 -4 -3 -2 -1 | +1

GTACAACTGC AGCAGCCTGG GGCTGAGCTG GTGAAGCCTG GGGCCTCAGT GAAGATGTCC 2520

TGCAAGGCTT CTGGCTACAC ATTTACCAGT TACAATATGC ACTGGGTAAA ACAGACACCT 2580

heavy chain variable = 363 bp = 121 A.A.

GGTCGGGGCC TGGAATGGAT TGGAGCTATT TATCCCGGAA ATGGTGATAC TTCCTACAAT 2640

CAGAAGTTCA AAGGCAAGGC CACATTGACT GCAGACAAAT CCTCCAGCAC AGCCTACATG 2700

CAGCTCAGCA GCCTGACATC TGAGGACTCT GCGGTCTATT ACTGTGCAAG ATCGACTTAC 2760

TACGGCGGTG ACTGGTACTT CAATGTCTGG GGCGCAGGGA CCACGGTCAC CGTCTCTGCA 2820

Nhe1 2820 | 1

GCTAGCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG 2880

GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG 2940

human gamma 1 constant = 993 bp

TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA 3000

330 AA + stop codon

GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC 3060

TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGCAGAGCCC 3120

AAATCTTGTG ACAAAACTCA CACATGCCCA CCGTGCCCAG CACCTGAACT CCTGGGGGGA 3180

CCGTCAGTCT TCCTCTTCCC CCCAAAACCC AAGGACACCC TCATGATCTC CCGGACCCCT 3240

GAGGTCACAT GCGTGGTGGT GGACGTGAGC CACGAAGACC CTGAGGTCAA GTTCAACTGG 3300

TACGTGGACG GCGTGGAGGT GCATAATGCC AAGACAAAGC CGCGGGAGGA GCAGTACAAC 3360

AGCACGTACC GTGTGGTCAG CGTCCTCACC GTCCTGCACC AGGACTGGCT GAATGGCAAG 3420

GAGTACAAGT GCAAGGTCTC CAACAAAGCC CTCCCAGCCC CCATCGAGAA AACCATCTCC 3480

Figure 3 (cont.)

AAAGCCAAAG GGCAGCCCCG AGAACCACAG GTGTACACCC TGCCCCCATC CCGGGATGAG 3540

CTGACCAAGA ACCAGGTCAG CCTGACCTGC CTGGTCAAAG GCTTCTATCC CAGCGACATC 3600

GCCGTGGAGT GGGAGAGCAA TGGGCAGCCG GAGAACAACT ACAAGACCAC GCCTCCCGTG 3660

CTGGACTCCG ACGGCTCCTT CTTCCTCTAC AGCAAGCTCA CCGTGGACAA GAGCAGGTGG 3720

CAGCAGGGGA ACGTCTTCTC ATGCTCCGTG ATGCATGAGG CTCTGCACAA CCACTACACG 3780

stop heavy chain | BamHI
CAGAAGAGCC TCTCCCTGTC TCCGGGTAAA TGA|GGATCCG TTAACGGTTA CCAACTACCT 3840
3813|4
linker # 7 = 816p

AGACTGGATT CGTGACAACA TGCGGCCGTG ATATCTACGT ATGATCAGCC TCGA|CTGTGC 3900
3894|5

CTTCTAGTTG CCAGCCATCT GTTGTTTGCC CCTCCCCCGT GCCTTCCTTG ACCCTGGAAG 3960

GTGCCACTCC CACTGTCCTT TCCTAATAAA ATGAGGAAAT TGCATCGCAT TGTCTGAGTA 4020

Bovine growth hormone polyadenylation region = 231 bp
GGTGTCATTC TATTCTGGGG GGTGGGGTGG GGCAGGACAG CAAGGGGGAG GATTGGGAAG 4080

linker # 8 = 346p
ACAATAGCAG GCATGCTGGG GATGCGGTGG GCTCTATGGA ACCAG|CTGGG GCTCGACAGC 4140
4125|6

GCTGGATCTC CCGATCCCCA GCTTTGCTTC TCAATTTCTT ATTTGCATAA TGAGAAAAAA 4200

AGGAAAATTA ATTTTAACAC CAATTCAGTA GTTGATTGAG CAAATGCGTT GCCAAAAAGG 4260

mouse Beta globin major promoter = 366 bp
ATGCTTTAGA GACAGTGTTC TCTGCACAGA TAAGGACAAA CATTATTCAG AGGGAGTACC 4320

CAGAGCTGAG ACTCCTAAGC CAGTGAGTGG CACAGCATTC TAGGGAGAAA TATGCTTGTC 4380

ATCACCGAAG CCTGATTCCG TAGAGCCACA CCTTGGTAAG GGCCAATCTG CTCACACAGG 4440

ATAGAGAGGG CAGGAGCCAG GGCAGAGCAT ATAAGGTGAG GTAGGATCAG TTGCTCCTCA 4500

linker #9 = 19 bp | 5' untranslated DHFR = 82bp
CATTTGCTTC TGACATAGTT GTGTT|GGGAG CTTGGATAGC TTGG|ACAGCT CAGGGCTGCG 4560
4525|6 4544|5

ATTTCGCGCC AAACTTGACG GCAATCCTAG CGTGAAGGCT GGTAGGATTT TATCCCCGCT 4620

start DHFR
GCCATC|ATG|G TTCGACCATT GAACTGCATC GTCGCCGTGT CCCAAAATAT GGGGATTGGC 4680
426|7

AAGAACGGAG ACCTACCCTG GCCTCCGCTC AGGAACGAGT TCAAGTACTT CCAAAGAATG 4740

ACCACAACCT CTTCAGTGGA AGGTAAACAG AATCTGGTGA TTATGGGTAG GAAAACCTGG 4800

DHFR = 564p = 187 amino acid + stop codon
TTCTCCATTC CTGAGAAGAA TCGACCTTTA AAGGACAGAA TTAATATAGT TCTCAGTAGA 4860

GAACTCAAAG AACCACCACG AGGAGCTCAT TTTCTTGCCA AAAGTTTGGA TGATGCCTTA 4920

AGACTTATTG AACAACCGGA ATTGGCAAGT AAAGTAGACA TGGTTTGGAT AGTCGGAGGC 4980

AGTTCTGTTT ACCAGGAAGC CATGAATCAA CCAGGCCACC TTAGACTCTT TGTGACAAGG 5040

ATCATGCAGG AATTTGAAAG TGACACGTTT TTCCCAGAAA TTGATTTGGG GAAATATAAA 5100

CTTCTCCCAG AATACCCAGG CGTCCTCTCT GAGGTCCAGG AGGAAAAAGG CATCAAGTAT 5160

STOP DHFR
AAGTTTGAAG TCTACGAGAA GAAAGA|CTAA|CAGGAAGATG CTTTCAAGTT CTCTGCTCCC 5220
5140|1

3' untranslated DHFR = 82 bp
linker # 10 = 10 bp
CTCCTAAAGC TATGCATTTT TATAAGACCA TGGGACTTTT GCTGGCTTTA GA|TCAGCCTC 5280
5272|3

GACTGTGCCT TCTAGTTGCC AGCCATCTGT TGTTTGCCCC TCCCCCGTGC CTTCCTTGAC 5340

Bovine growth hormone polyadenylation = 2316p

CCTGGAAGGT GCCACTCCCA CTGTCCTTTC CTAATAAAAT GAGGAAATTG CATCGCATTG 5400

TCTGAGTAGG TGTCATTCTA TTCTGGGGGG TGGGGTGGGG CAGGACAGCA AGGGGGAGGA 5460

linker # 11 = 17 bp

TTGGGAAGAC AATAGCAGGC ATGCTGGGGA TGCGGTGGGC TCTATGGAAC CAGCTGGGGC 5520

5513 | 4

TCGAGCTACT | AGCTTTGCTT CTCAATTTCT TATTTGCATA ATGAGAAAAA AAGGAAAATT 5580

5530 | 1

AATTTTAACA CCAATTCAGT AGTTGATTGA GCAAATGCGT TGCCAAAAAG GATGCTTTAG 5640

Mouse beta globin major promoter = 366 bp

AGACAGTGTT CTCTGCACAG ATAAGGACAA ACATTATTCA GAGGGAGTAC CCAGAGCTGA 5700

GACTCCTAAG CCAGTGAGTG GCACAGCATT CTAGGGAGAA ATATGCTTGT CATCACCGAA 5760

GCCTGATTCC GTAGAGCCAC ACCTTGGTAA GGGCCAATCT GCTCACACAG GATAGAGAGG 5820

GCAGGAGCCA GGGCAGAGCA TATAAGGTGA GGTAGGATCA GTTGCTCCTC ACATTTGCTT 5880

linker # 12 = 21 bp

start neo

CTGACATAGT TGTGTT | GGGA GCTTGGATCG ATCCTCTATG GTTGAACAAG ATGGATTGCA 5940

5896 | 7

5917 | 8

CGCAGGTTCT CCGGCCGCTT GGGTGGAGAG GCTATTCGGC TATGACTGGG CACAACAGAC 6000

AATCGGCTGC TCTGATGCCG CCGTGTTCCG GCTGTCAGCG CAGGGGCGCC CGGTTCTTTT 6060

Neomycin phosphotransferase = 795 bp = 264 AA + stop codon

TGTCAAGACC GACCTGTCCG GTGCCCTGAA TGAACTGCAG GACGAGGCAG CGCGGCTATC 6120

GTGGCTGGCC ACGACGGGCG TTCCTTGCGC AGCTGTGCTC GACGTTGTCA CTGAAGCGGG 6180

AAGGGACTGG CTGCTATTGG GCGAAGTGCC GGGGCAGGAT CTCCTGTCAT CTCACCTTGC 6240

TCCTGCCGAG AAAGTATCCA TCATGGCTGA TGCAATGCGG CGGCTGCATA CGCTTGATCC 6300

GGCTACCTGC CCATTCGACC ACCAAGCGAA ACATCGCATC GAGCGAGCAC GTACTCGGAT 6360

GGAAGCCGGT CTTGTCGATC AGGATGATCT GGACGAAGAG CATCAGGGGC TCGCGCCAGC 6420

CGAACTGTTC GCCAGGCTCA AGGCGCGCAT GCCCGACGGC GAGGATCTCG TCGTGACCCA 6480

TGGCGATGCC TGCTTGCCGA ATATCATGGT GGAAAATGGC CGCTTTTCTG GATTCATCGA 6540

CTGTGGCCGG CTGGGTGTGG CGGACCGCTA TCAGGACATA GCGTTGGCTA CCCGTGATAT 6600

TGCTGAAGAG CTTGGCGGCG AATGGGCTGA CCGCTTCCTC GTGCTTTACG GTATCGCCGC 6660

STOP NEO

TCCCGATTCG CAGCGCATCG CCTTCTATCG CCTTCTTGAC GAGTTCTTCT GAGCGGGACT 6720

6712 | 3

CTGGGGTTCG AAATGACCGA CCAAGCGACG CCCAACCTGC CATCACGAGA TTTCGATTCC 6780

3' untranslated Neo = 173 bp

ACCGCCGCCT TCTATGAAAG GTTGGGCTTC GGAATCGTTT TCCGGGACGC CGGCTGGATG 6840

ATCCTCCAGC GCGGGGATCT CATGCTGGAG TTCTTCGCCC ACCCCAACTT GTTTATTGCA 6900

6885 | 6

GCTTATAATG GTTACAAATA AAGCAATAGC ATCACAAATT TCACAAATAA AGCATTTTTT 6960

SV40 early polyadenylation region = 1336p

TCACTGCATT CTAGTTGTGG TTTGTCCAAA CTCATCAATC TATCTTATCA TGTCTGGATC 7020

7018 | 9

linker # 13 = 19 bp

GCGGCCGCGA TCCCGTCGAG AGCTTGGCGT AATCATGGTC ATAGCTGTTT CCTGTGTGAA 7080

7037 | 8

Puc 19

Puc 19

ATTGTTATCC GCTCACAATT CCACACAACA TACGAGCCGG AAGCATAAAG TGTAAAGCCT 7140

GGGGTGCCTA ATGAGTGAGC TAACTCACAT TAATTGCGTT GCGCTCACTG CCCGCTTTCC 7200

AGTCGGGAAA CCTGTCGTGC CAGCTGCATT AATGAATCGG CCAACGCGCG GGGAGAGGCG 7260

GTTTGCGTAT TGGGCGCTCT TCCGCTTCCT CGCTCACTGA CTCGCTGCGC TCGGTCGTTC 7320

GGCTGCGGCG AGCGGTATCA GCTCACTCAA AGGCGGTAAT ACGGTTATCC ACAGAATCAG 7380

GGGATAACGC AGGAAAGAAC ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCGTAAAA 7440

7461 = bacterial origin of replication

AGGCCGCGTT GCTGGCGTTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC 7500

GACGCTCAAG TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG GCGTTTCCCC 7560

CTGGAAGCTC CCTCGTGCGC TCTCCTGTTC CGACCCTGCC GCTTACCGGA TACCTGTCCG 7620

CCTTTCTCCC TTCGGGAAGC GTGGCGCTTT CTCAATGCTC ACGCTGTAGG TATCTCAGTT 7680

CGGTGTAGGT CGTTCGCTCC AAGCTGGGCT GTGTGCACGA ACCCCCCGTT CAGCCCGACC 7740

GCTGCGCCTT ATCCGGTAAC TATCGTCTTG AGTCCAACCC GGTAAGACAC GACTTATCGC 7800

CACTGGCAGC AGCCACTGGT AACAGGATTA GCAGAGCGAG GTATGTAGGC GGTGCTACAG 7860

AGTTCTTGAA GTGGTGGCCT AACTACGGCT ACACTAGAAG GACAGTATTT GGTATCTGCG 7920

CTCTGCTGAA GCCAGTTACC TTCGGAAAAA GAGTTGGTAG CTCTTGATCC GGCAAACAAA 7980

CCACCGCTGG TAGCGGTGGT TTTTTTGTTT GCAAGCAGCA GATTACGCGC AGAAAAAAAG 8040

GATCTCAAGA AGATCCTTTG ATCTTTTCTA CGGGGTCTGA CGCTCAGTGG AACGAAAACT 8100

CACGTTAAGG GATTTTGGTC ATGAGATTAT CAAAAAGGAT CTTCACCTAG ATCCTTTTAA 8160

8219 = stop Beta lactamase

ATTAAAAATG AAGTTTTAAA TCAATCTAAA GTATATATGA GTAAACTTGG TCTGACAGTT 8220

ACCAATGCTT AATCAGTGAG GCACCTATCT CAGCGATCTG TCTATTTCGT TCATCCATAG 8280

TTGCCTGACT CCCCGTCGTG TAGATAACTA CGATACGGGA GGGCTTACCA TCTGGCCCCA 8340

GTGCTGCAAT GATACCGCGA GACCCACGCT CACCGGCTCC AGATTTATCA GCAATAAACC 8400

Beta lactamase = 861bp = 286 A.A + stop codon

AGCCAGCCGG AAGGGCCGAG CGCAGAAGTG GTCCTGCAAC TTTATCCGCC TCCATCCAGT 8460

CTATTAATTG TTGCCGGGAA GCTAGAGTAA GTAGTTCGCC AGTTAATAGT TTGCGCAACG 8520

TTGTTGCCAT TGCTACAGGC ATCGTGGTGT CACGCTCGTC GTTTGGTATG GCTTCATTCA 8580

GCTCCGGTTC CCAACGATCA AGGCGAGTTA CATGATCCCC CATGTTGTGC AAAAAAGCGG 8640

TTAGCTCCTT CGGTCCTCCG ATCGTTGTCA GAAGTAAGTT GGCCGCAGTG TTATCACTCA 8700

TGGTTATGGC AGCACTGCAT AATTCTCTTA CTGTCATGCC ATCCGTAAGA TGCTTTTCTG 8760

TGACTGGTGA GTACTCAACC AAGTCATTCT GAGAATAGTG TATGCGGCGA CCGAGTTGCT 8820

CTTGCCCGGC GTCAATACGG GATAATACCG CGCCACATAG CAGAACTTTA AAAGTGCTCA 8880

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TCATTGGAAA ACGTTCTTCG GGGCGAAAAC TCTCAAGGAT CTTACCGCTG TTGAGATCCA   8940

GTTCGATGTA ACCCACTCGT GCACCCAACT GATCTTCAGC ATCTTTTACT TTCACCAGCG   9000

TTTCTGGGTG AGCAAAAACA GGAAGGCAAA ATGCCGCAAA AAAGGGAATA AGGGCGACAC   9060
                  9079 = start beta lactamase
GGAAATGTTG AATACTCATA CTCTTCCTTT TTCAATATTA TTGAAGCATT TATCAGGGTT   9120

ATTGTCTCAT GAGCGGATAC ATATTTGAAT GTATTTAGAA AAATAAACAA ATAGGGGTTC   9180

CGCGCACATT TCCCCGAAAA GTGCCACCT
```

FIGURE 4

Leader

```
                    -20                 -15                 -10
Frame 1  Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val
         ATG GAT TTT CAG GTG CAG ATT ATC AGC TTC CTG CTA ATC AGT GCT TCA GTC
                  987         996         1005        1014        1023

 -5                -1 | +1     FR1                             10
 Ile Met Ser Arg Gly | Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser
 ATA ATG TCC AGA GGA | CAA ATT GTT CTC TCC CAG TCT CCA GCA ATC CTG TCT GCA TCT
        1038        1047        1056        1065        1074        1083

                        20          23 | 24     CDR1    27/ 29  30          34 |
 Pro Gly Glu Lys Val Thr Met Thr Cys | Arg Ala Ser Ser Ser Val Ser Tyr Ile His |
 CCA GGG GAG AAG GTC ACA ATG ACT TGC | AGG GCC AGC TCA AGT GTA AGT TAC ATC CAC |
        1095        1104        1113 |       1122        1131        1140      |

 35     FR2          40                  45              49 | 50     CDR2
 Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr | Ala Thr Ser Asn
 TGG TTC CAG CAG AAG CCA GGA TCC TCC CCC AAA CCC TGG ATT TAT | GCC ACA TCC AAC
        1152        1161        1170        1179        1188|       1197

    55  56 | 57          60       FR3        65                  70
 Leu Ala Ser | Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser
 CTG GCT TCT | GGA GTC CCT GTT CGC TTC AGT GGC AGT GGG TCT GGG ACT TCT TAC TCT
        1209 |       1218        1227        1236        1245        1254

          75                  80                  85          88 | 89  90
 Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys | Gln Gln Trp
 CTC ACA ATC AGC AGA GTG GAG GCT GAA GAT GCT GCC ACT TAT TAC TGC | CAG CAG TGG
        1266        1275        1284        1293        1302    |   1311

      CDR3  95      97 | 98     100  FR4            105     107 |
 Thr Ser Asn Pro Pro Thr | Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys |
 ACT AGT AAC CCA CCC ACG | TTC GGA GGG GGG ACC AAG CTG GAA ATC AAA |
        1323        1332 |       1341        1350        1359    |
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ATTACHMENT B

08/149099

A/ ... Sequence

THERAPEUTIC APPLICATION OF CHIMERIC AND RADIOLABELED ANTIBODIES TO HUMAN B LYMPHOCYTE RESTRICTED DIFFERENTIATION ANTIGEN FOR TREATMENT OF B CELL LYMPHOMA

Darrell R. Anderson, Nabil Hanna, John E. Leonard
Roland A. Newman, Mitchell E. Reff and William H. Rastetter

RELATED APPLICATIONS

This is a Continuation-in-Part of United States Serial No. ~~07/978,891, filed November 13, 1992, pending.~~ This patent document is related to United States Serial No. 07/977,691, (now abandoned) entitled "IMPAIRED DOMINANT SELECTABLE MARKER SEQUENCE FOR ENHANCEMENT OF EXPRESSION OF CO-LINKED GENE PRODUCT AND EXPRESSION VECTOR SYSTEMS COMPRISING SAME" having U.S. Serial No. 07/977,691 (~~pending~~ now abandoned; filed November 13, 1992) and "IMPAIRED DOMINANT SELECTABLE MARKER SEQUENCE AND INTRONIC INSERTION STRATEGIES FOR ENHANCEMENT OF EXPRESSION OF GENE PRODUCT AND EXPRESSION VECTOR SYSTEMS COMPRISING SAME," U.S. Serial No. ~~08/~~ 08/147,696 (now US Patent 564824) (filed simultaneously herewith). The related patent documents are incorporated herein by reference.

~~This document is being filed in accordance with Rule 10.~~
~~EXPRESS MAIL LABEL NO.:~~
~~DATE OF DEPOSIT:~~

ATTACHMENT C

US005736137A

United States Patent [19]

Anderson et al.

[11] Patent Number: 5,736,137

[45] Date of Patent: Apr. 7, 1998

[54] **THERAPEUTIC APPLICATION OF CHIMERIC AND RADIOLABELED ANTIBODIES TO HUMAN B LYMPHOCYTE RESTRICTED DIFFERENTIATION ANTIGEN FOR TREATMENT OF B CELL LYMPHOMA**

[75] Inventors: **Darrell R. Anderson**, Escondido; **Nabil Hanna**, Olivenhain; **John E. Leonard**, Encinitas; **Roland A. Newman**; **Mitchell E. Reff**, both of San Diego; **William H. Rastetter**, Rancho Sante Fe, all of Calif.

[73] Assignee: **Idec Pharmaceuticals Corporation**, San Diego, Calif.

[21] Appl. No.: **149,099**

[22] Filed: **Nov. 3, 1993**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 978,891, Nov. 13, 1992, abandoned.

[51] **Int. Cl.**[6] **A61K 39/395**; C07K 16/30; C12N 1/21; C12N 5/20

[52] **U.S. Cl.** **424/133.1**; 424/143.1; 424/144.1; 424/156.1; 424/174.1; 424/800; 424/801; 424/153.1; 435/320.1; 435/328; 435/334; 435/343.1; 435/252.3; 435/70; 435/72; 435/15; 435/104; 530/387.3; 530/388.22; 530/388.73; 530/388.85; 530/867

[58] **Field of Search** 424/133.1, 143.1, 424/144.1, 156.1, 174.1, 800, 801, 153.1; 435/69.6, 172.3, 252.3, 320.1, 240.2, 328, 334, 343.1; 536/23.4, 23.5, 23.53; 530/387.3, 388.22, 388.73, 388.85, 867; 935/70, 72, 15, 104

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Primary Examiner—Ronald B. Schwadron

Attorney, Agent, or Firm—Burns, Doane, Swecker & Mathis, LLP

[57] **ABSTRACT**

Disclosed herein are therapeutic treatment protocols designed for the treatment of B cell lymphoma. These protocols are based upon therapeutic strategies which include the use of administration of immunologically active mouse/human chimeric anti-CD20 antibodies, radiolabeled anti-CD20 antibodies, and cooperative strategies comprising the use of chimeric anti-CD20 antibodies and radiolabeled anti-CD20 antibodies.

6 Claims, 21 Drawing Sheets

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No.:	**07/ 978,891**	Group Art Unit:	1644
Confirmation No.:	4493	Examiner:	R.B. Schwadron
Filed:	13 November 1992		
Applicant:	Darrell R. ANDERSON *et al.*		

For: Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma

Mail Stop **Petition**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.183

Sir:

Applicant is filing concurrently in this application a petition under 37 C.F.R. § 1.137(b) to revive the abandoned application on the basis of unintentional delay in filing a reply for the sole purpose of establishing copendency with a continuing application. Section 1.137(b)(4) requires, as one component of a petition under § 1.137(b), a terminal disclaimer pursuant to § 1.137(d).

Applicant petitions the Director to waive the requirement of § 1.137(b)(4) for the submission of a terminal disclaimer in connection with the concurrently-filed petition to revive, as discussed at M.P.E.P. § 711.03(c), subsection II.G.

Applicant requests that the Director debit that fee of **$400** (§1.17(f)) from our **Deposit Account No. 18-1260**. Any other fee required for entry or consideration of this paper may be charged to the same account.

Facts

1. As explained in the concurrently-filed petition under § 1.137, application serial no. 07/978,891 may have become abandoned on 16 September 1993 for applicant's failure to file a timely reply to the nonfinal Office action mailed 15 June 1993.

2. Application serial no. 08/149,099 was filed on 3 November 1993 as a continuation-in-part of the '891 application. The '099 application matured to U.S. Patent No. 5,736,137 on 7 April 1998.

3. Several other applications and patents claiming priority under 35 U.S.C. § 120 to the '891 and '099 applications have been filed and prosecuted between 1993 and 2007, including U.S. Patent Nos. 5,736,137, 5,776,456, 5,843,439, 6,399,061, and 6,682,734, as well as pending application serial nos. 09/911,692, 09/911,703, and 10/238,681.

Discussion

Section 1.137(b)(4) requires that a patentee or applicant seeking to revive an abandoned application in certain circumstances must submit a terminal disclaimer as specified in § 1.137(d). Section 1.137(d)(1) provides that a petition to revive an application filed before 8 June 1995 should be accompanied by a terminal disclaimer for the lesser of the period of abandonment (*i.e.*, up to the date a petition to revive is granted) or the period beyond 20 years from the earliest claimed filing date.

Section 1.183 provides that the Director may waive any requirement of the regulations which is not a requirement of the statutes "[i]n an extraordinary situation, when justice requires." The provision of § 1.137(b)(4) is mandated solely by the rules and is not a requirement of the statute. Accordingly, the Directory has authority to waive this requirement pursuant to § 1.183.

The terminal disclaimer requirement of § 1.137(b) is discussed at M.P.E.P. § 711.03(c), subsection II.G. That section of the Manual states:

> In the event that an applicant considers the requirement for a terminal disclaimer to be inappropriate under the circumstances of the application at issue, the applicant should file a petition under 37 CFR 1.183 (and petition fee) to request a waiver .... The grant of such a petition, however, is strictly limited to situations wherein applicant has made a showing of an "extraordinary situation" in which "justice requires" the requested relief. An example of such a situation is when the abandonment of the application caused no actual delay in prosecution ... .

In this instance, the abandonment of the application did not lead to a delay in prosecution. The continuing application filed on 3 November 1993, serial no. 08/149,099, represents a complete reply to the outstanding Office action within the meaning of § 1.137. *See* M.P.E.P. § 711.03(c), subsection II.A. This application was filed within the period permitted by statute for reply to the outstanding Office action. Indeed, the '099 application had already been on file for more than a month when the examiner contacted applicant to inquire about the status of the '891 application. *See* interview summary dated 7 December 1993 (Paper No. 13). The '099 application was regularly processed and taken up for examination in turn, with no delay attributable to the period of abandonment in the parent application.

These facts suffice to demonstrate a showing of an extraordinary situation, where justice requires the requested relief, as set forth at M.P.E.P. § 711.03(c), subsection II.A. This is all the more so when the events in question occurred some 14 years ago, and applicant has since obtained patents with no reason to expect that the claim for priority to the original application under § 120 would not be effective.

* * *

6-22-1091

Conclusion

Applicant respectfully requests that the Director waive the requirement of § 1.137(b)(4) for submission of a terminal disclaimer in connection with the concurrently-filed petition to revive application serial no. 07/978,891 for copendency with application serial no. 08/149,099.

Respectfully submitted,

/David L. Fitzgerald/

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7 November 2007

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No.:	**07/ 978,891**	Group Art Unit:	1644
Confirmation No.:	4493	Examiner:	R.B. Schwadron
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Mail Stop **Petition**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.137(b) TO REVIVE

AN UNINTENTIONALLY ABANDONED APPLICATION FOR COPENDENCY

Sir:

In connection with the recent evaluation of a petition in a pending application (serial no. 09/911,703) that claims priority to the captioned application, serial no. 07/978,891, it has come to applicant's attention that application serial no. 07/978,891 may have become abandoned through unintentional delay before a continuing application, serial no. 08/149,099, now U.S. Patent No. 5,736,137, was filed. In particular, the '891 application may have become abandoned as early as 16 September 1993, whereas the '099 application was filed as a continuation-in-part of the '891 application on 3 November 1993. The record demonstrates that applicant intended, and the Office proceeded under the assumption, that the '099 application was filed prior to the abandonment of the '891 application. Accordingly, applicant petitions under 37 C.F.R. § 1.137(b) to revive the captioned '891 application solely for the purpose of establishing copendency with the '099 application.

The Director is requested to debit the required petition fee of **$1,540** (§ 1.17(m)) from our **Deposit Account No. 18-1260.** Any other fee required for entry or consideration of this paper may be charged to the same account.

This petition is submitted with a concurrently-filed petition under § 1.183 to waive the terminal disclaimer requirement of § 1.137(b)(4), as discussed at M.P.E.P. § 711.03(c), subsection II.G.

Conclusion

Applicant respectfully requests that application serial no. 07/978,891 be revived solely to establish copendency with application serial no. 08/149,099, filed on 3 November 1993, and that once such copendency has been established, the application again be abandoned.

Respectfully submitted,

/David L. Fitzgerald/

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7 November 2007

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